Diagnosis and Management of Retroperitoneal Soft-tissue Sarcoma

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Retroperitoneal soft-tissue sarcomas are locally invasive tumors that remain occult for long periods and grow quite large due to the abdominal cavity's remarkable ability to accommodate these slowly expanding masses with a paucity of attendant symptoms. An open biopsy is required to establish diagnosis definitively. Despite improved imaging techniques and preoperative and intraoperative patient management, resectability has not changed significantly in the past 20 years. Even with an aggressive operative approach, only one half the tumors can be resected completely, and of those, more than 90% recur locally and result in the death of the patient. The addition of adjuvant radiotherapy or chemotherapy has not altered this pattern of local failure, in contrast to promising results with extremity soft-tissue sarcoma. Because of the rarity of these tumors, there is an urgent need to establish a national retroperitoneal sarcoma registry and to form cooperative intergroup studies to evaluate, treat, and apply innovative multimodality combination therapies to these otherwise lethal tumors.

RETROPERITONEAL SOFT-TISSUE sarcomas are comprised of a heterogenous group of rare and capricious mesenchymal neoplasms. Soft-tissue sarcomas account for 1% of all solid tumors, with an incidence of approximately 2 in 100,000, or about 6000 new cases in the United States per year. Of these 15% will occur in the retroperitoneum (1000 cases per year). These tumors have a well-earned reputation for regional invasion and local recurrence and have humbled many a skilled surgeon. But, in fact, it is the surgeon who has the greatest likelihood of rendering such patients disease free, and it is for this reason that general surgeons must take the time and effort to understand fully and appreciate the biologic nature of these unusual neoplasms. While no large prospective randomized clinical trials exist, accumulative past experience clearly illustrates several important principles of management.

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Presentation and Differential Diagnosis

Retroperitoneal sarcomas have a peak incidence in the fifth decade of life, although they have occurred in patients in their teens. In patients (n = 675)[1] with a retroperitoneal neoplasm, 82% were malignant and 18% benign. Of those with malignancy, 40% were lymphoma or some variety of urogenital cancer and 55% were sarcoma. Stated another way, nearly one half of all retroperitoneal solid neoplasms will prove to be soft-tissue sarcoma.

Patients most frequently present with a nontender palpable mass (80% to 90%). They may give a history of increasing abdominal girth and frequently (40% to 70%) describe vague poorly localized discomfort due to stretching of the peritonea. One third of patients will have some distal neurologic sign or symptom from the mass effect, stretching or compressing the lumbar or pelvic nerve plexes. Less commonly nonmalignant serous ascites due to external portal vein obstruction, and gastrointestinal symptoms of a partially obstructive nature due to displacement or direct invasion by the expanding mass are found in 15% and 10% of patients, respectively.

In those patients in whom tumor necrosis has occurred, a rather constant low-grade fever is common and often accompanied by mild leukocytosis. If tumor erosion into a hollow viscus has occurred, the patient may present with acute or chronic gastrointestinal bleeding. Very rarely patients may manifest hypoglycemia, either due to the production of insulinlike substances by some poorly differentiated sarcomas, or more rapid use of glucose stores by some metabolically active larger sarcomas. Most symptoms of this disease therefore are subtle not pathognomonic and only bring the patient to medical attention late in the course of the disease.[2]

Evaluation of a Retroperitoneal Mass

Abdominal masses generally can be diagnosed by a careful history and physical examination combined with radiographic studies, such as upper gastrointestinal series, barium enema, intravenous pyelogram, and chest x-ray; these studies also will often provide valuable additional information if the diagnosis of sarcoma is made later.

The most definitive single radiographic study is an abdominal computed tomography (CT) scan. The CT will establish the solid composition, the presence or absence of necrosis, evidence of liver metastases, and the retroperitoneal location of such tumors. Because mesenchymal tumors frequently are heterogenous and comprised of irregular solid, semisolid, and liquefactive areas due to patchy necrosis, sarcoma may be highly suspect based on this study alone (Fig. 1).[3] The abdominal CT scan also will be valuable in differentiating sarcomas from other retroperitoneal malignancies, such as lymphoma manifesting multinodal involvement, where lymph node or bone marrow biopsy may be diagnostic, or urogenital tumors that tend to be more homogenous where germ cell markers (*i.e.*, αFP, βHCG) or testicular ultrasound may preclude laparotomy.

If the diagnosis of sarcoma seems likely, or remains possible, an abdominal magnetic resonance image (MRI) scan may better delineate the nature and extent of the neoplasm. Overview coronal sections may show the location and patency of the vena cava (Fig. 2). The T_1-weighted MRI image (Fig. 3) often will better define the relationship of the tumor to other solid organs (*e.g.*, liver, spleen, kidney). The T_2-weighted MRI image will best indicate adjacent muscle invasion and is particularly useful in determining the extent of tumor within the psoas or quadratus muscles and those tumors alarmingly near the spinal foramena (Fig. 4).

If the index of suspicion for sarcoma remains high, an aortogram, with or without venacavogram, depending on the location of the tumor, is often warranted (Fig. 5).[4] Sarcomas tend to be quite vascular neoplasms and knowledge of the extent and location of tumor-feeding vessels are important aids for operative planning. Displacement, encasement, and/or direct invasion of normal vessels may be delineated. The aortogram also will evaluate renal function should the patient require unilateral nephrectomy.

Finally, before biopsy, a chest CT scan should be obtained to rule out pulmonary metastases. Retroperitoneal sarcomas have an equal chance of metastasizing to liver or lung. Not infrequently pulmonary metastases from soft-tissue sarcomas occur only in the lung periphery and are not seen on plain chest x-ray. Chest CT often will disclose peripheral metastases of 1 cm or less (Fig. 6), which could influence future operative management.

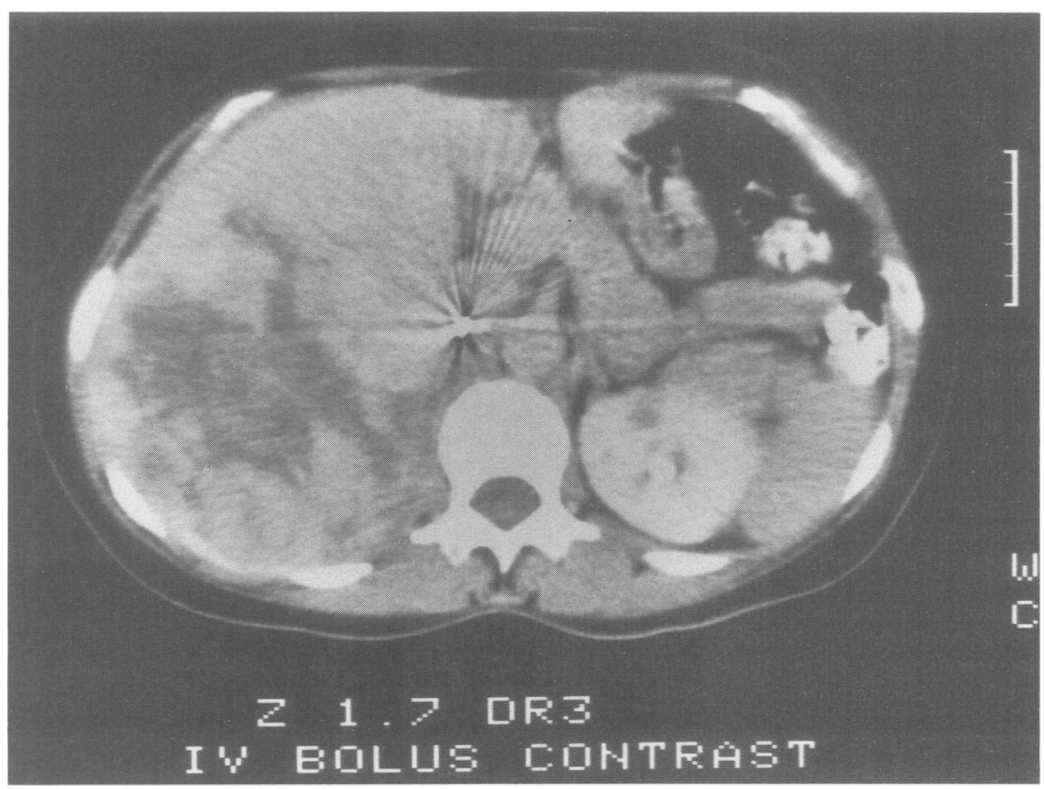

FIG. 1. Abdominal computed tomography scan of retroperitoneal sarcoma indicating its heterogenous nature.

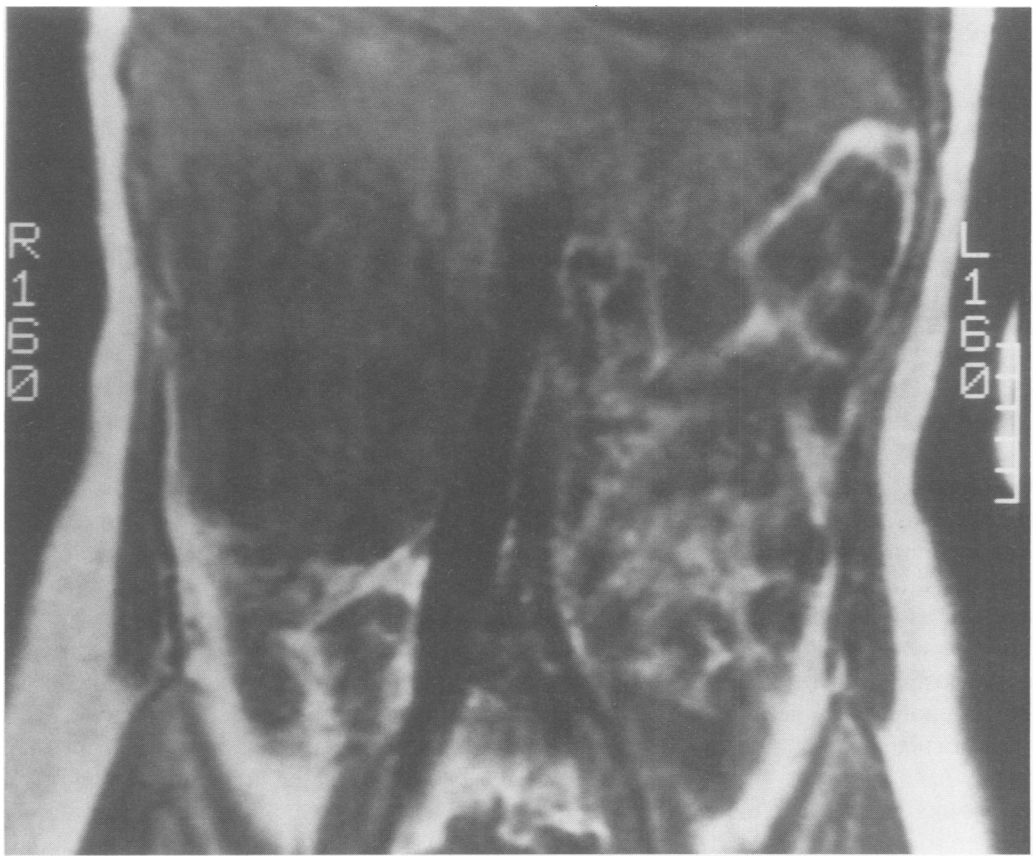

FIG. 2. Magnetic resonance imaging scan, overview coronal section, of retroperitoneal sarcoma shown in Figure 1 indicating patency of the vena cava.

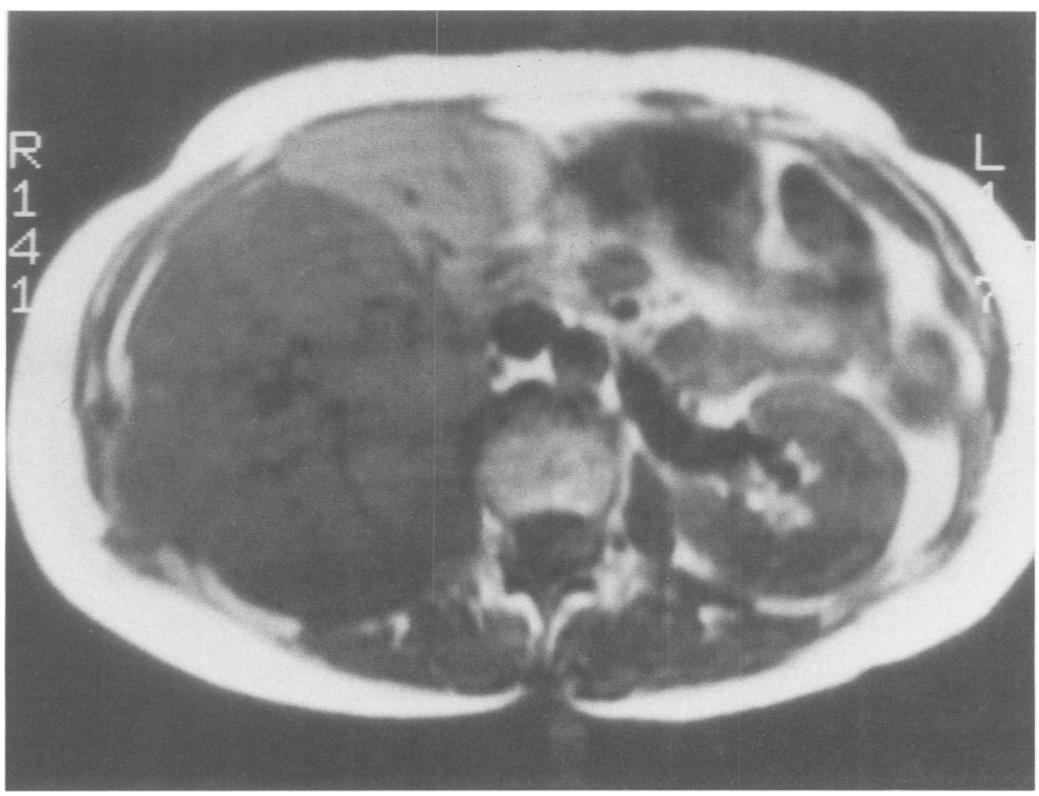

FIG. 3. T1-weighted magnetic resonance imaging scan defining relationship of retroperitoneal sarcoma shown in Figure 1 to adjacent solid organs.

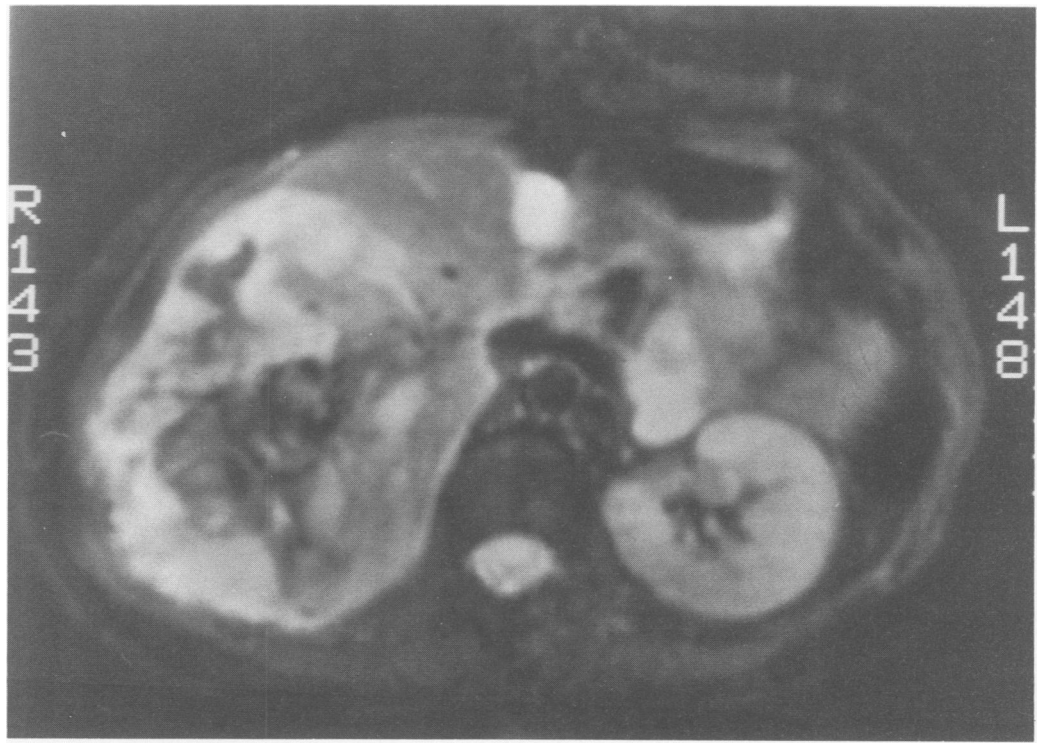

FIG. 4. T2-weighted magnetic resonance imaging scan defining relationship of retroperitoneal sarcoma shown in Figure 1 to adjacent muscle and spinal foramena.

Biopsy of a Retroperitoneal Mass

Ultrasound or CT-guided fine-needle aspiration biopsy or core needle biopsy (*e.g.*, Tru-cut™, Travenol Laboratories, Delfied, IL) often is warranted in confirming deposits of abdominal metastases of other cancers and for diagnosing isolated defects within the liver, adrenal glands, and so on. However these biopsy techniques rarely yield enough useful tissue to provide the information necessary to manage primary retroperitoneal neoplasms successfully, whether they are sarcomas, lymphomas, or urogenital neoplasms. Thus, in the absence of compelling reasons to the contrary, open biopsy is indicated.

In one study of patients with retroperitoneal sarcoma, none manifested intra-abdominal sarcomatosis without having previously undergone biopsy,[2] the implication being that the technique of biopsy is critical in preventing peritoneal seeding of tumor. Laparotomy under general anesthesia is warranted. Wound edges should be protected with plastic barriers. The most solid portion of the tumor should be isolated with a liberal use of laparotomy pads and all normal structures packed off. The tumor capsule should be incised carefully and a 1- to 2-cc wedge of underlaying tumor excised, then the capsule meticulously reapproximated with fine sutures after complete tumor hemostasis has been achieved. Every precaution should be used to prevent free tumor spill or tumor spread *via* an expanding hematoma. The tumor should be sent fresh to the pathologist for 'touch preps' and frozen section on a portion of the sample. In many cases, even though sufficient viable tumor tissue is present for diagnosis, a definitive diagnosis cannot be rendered with certainty by frozen section due to freezing artifact. In this circumstance the operation should be terminated. Treatment should await permanent sections and special stains and electron microscopy as needed. Further dissection or any form of

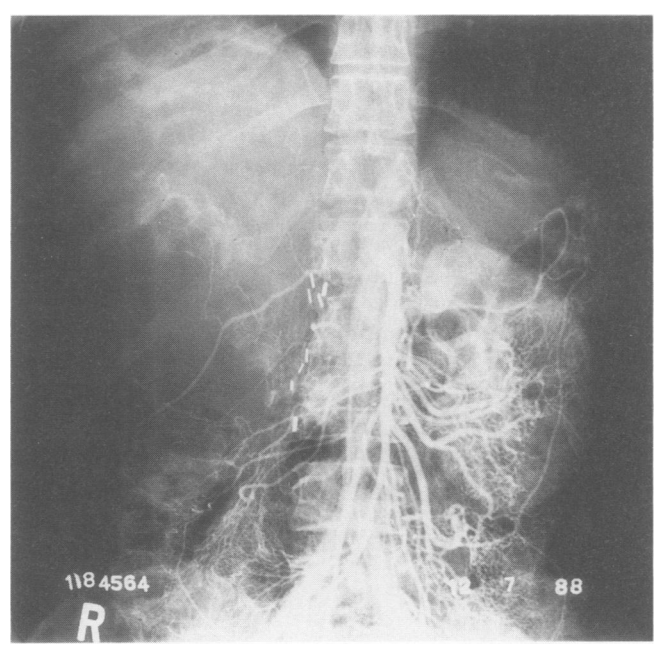

FIG. 5. Aortogram of retroperitoneal sarcoma shown in Figure 1 indicating location and extent of tumor feeding vessels.

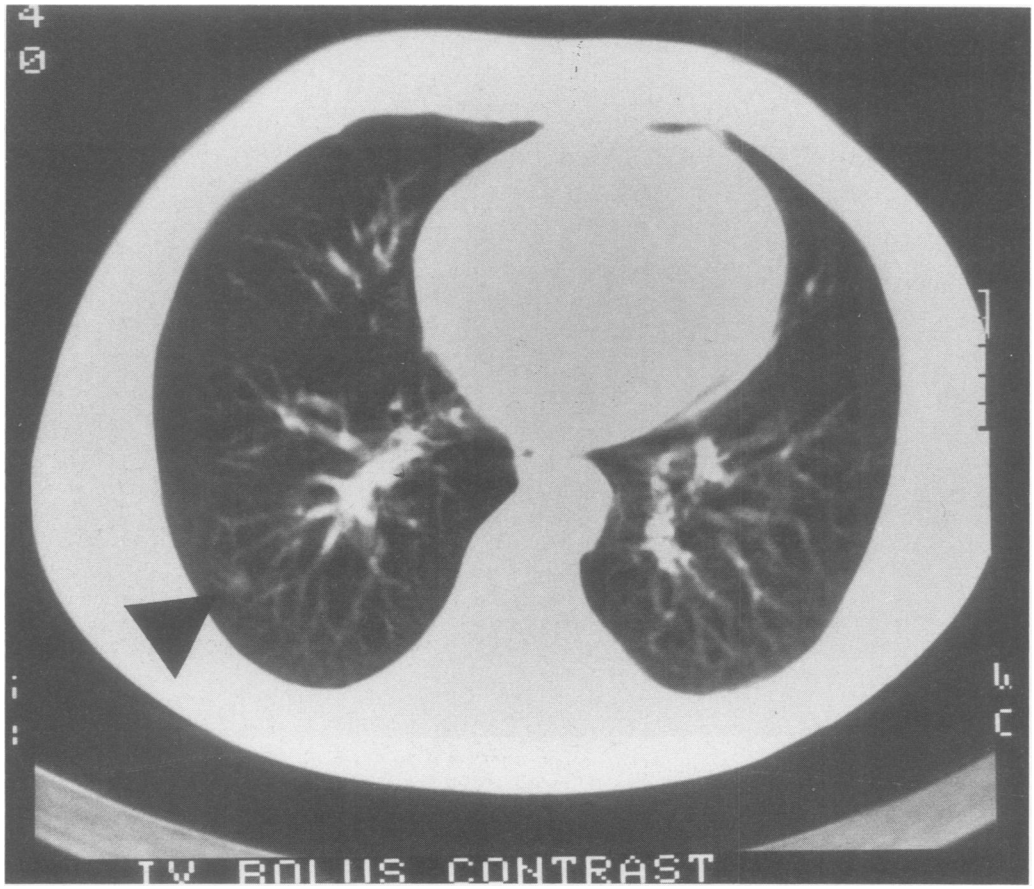

FIG. 6. Chest computed tomograph, lung windows, indicating presence of a 1-cm sarcoma peripheral lung metastasis not seen on plain chest x-ray.

resection is contraindicated in the absence of a definitive diagnosis because such maneuvers inadvertently may expose normal tissue planes to sarcoma, making a subsequent curative resection less likely.

Tumor Histology and Patient Staging

Based on cumulative series (n = 449),[1] the most common retroperitoneal sarcomas are, in descending order of frequency, liposarcoma, fibrosarcoma, leiomyosarcoma, undifferentiated sarcoma, neurosarcoma, and other less common sarcomas (Table 1). Conspicuous by its absence from this list is malignant fibrous histiocytoma, which is a more recent designation being used with greater and greater frequency to identify mesenchymal tumors at all locations but that was not used in most historic series. It is not the variety of sarcoma but rather the histopathologic grade of malignancy, however, that has the greatest bearing on prognosis.

TABLE 1. *Retroperitoneal Sarcoma*

Histology	Incidence (%)*
Liposarcoma	23
Fibrosarcoma	19
Leiomyosarcoma	16
Neurosarcoma	12
Undifferentiated	16
Other, various	14

* Combined series, n = 449.

Sarcomas are designated as grade 1, G1 (well differentiated), grade 2, G2 (intermediate grade, moderately well differentiated), or grade 3, G3 (poorly differentiated or undifferentiated) depending on the degree of cytologic atypia, number of mitoses, and presence and extent of necrosis. Tumors measuring less than 5 cm are designated T1, ≥ 5 cm are T2, and those with bone, nerve, or vascular invasion were classified T3 in older schema.

Staging of patients with soft-tissue sarcoma has been in transition in the past decade. As a general rule, the histopathologic grade of the tumor determines the stage of the patient's disease (Table 2). A patient with a G1 sarcoma is stage I, and so on. Patients with a 'T1' tumor less than 5 cm are substage A; those with larger tumors are substage B. In some past schemas, patients with regionally invasive (T3) tumors were classified as substage IV A; currently stage IV A identifies patients with lymph node metastases and IV B identifies patients with distant metastases.

TABLE 2. *Sarcoma Staging*

Tumor Designation	Tumor Histopathology	Tumor Grade	Patient Stage
G1	Well differentiated	Low	I
G1	Mod. well differentiated	Intermediate	II
G3	Poorly differentiated; undifferentiated	High	III

<5 cm = T1 tumor; substage A.
≥5 cm = T2 tumor; substage B.
(Bone, nerve, vessel invasion = T3 tumor; substage IVA in past schemas).
Currently stage IVA designates patients with nodal metastases; IVB denotes distant disease.

Operative Techniques

Incisions

Long midline or diagonal 'saber slash' incisions are used to provide optimum exposure to retroperitoneal sarcomas, either of which may be extended into the chest as needed. It should be remembered that sarcomas tend to be highly vascular neoplasms whose blood supply almost invariably arises from the midline (Fig. 5). Early control of these midline vessels is mandatory, which is virtually impossible *via* flank approaches. The flank approach is mentioned in this context only to be condemned because it is one of the important contributory factors to poor exposure, inadequate vascular control, unrelenting hemorrhage, and tumor dehiscence.

Evaluation of Resectability

Retroperitoneal sarcomas tend to be either right sided or left sided, with few actually arising from midline structures. Unfortunately the retroperitoneum is not compartmentalized like the extremity, and as a consequence there are no significant fascial barriers to contain the neoplasm. The first maneuver in determining resectability requires dissection, often in a subadventitial plane, along the lateral border of the aorta or vena cava, extended dorsally between the spine and psoas/quadratus muscles (Fig. 7). This critical first step will determine whether the tumor has traversed along a spinal nerve root into the spinal foramena and into the cord, the presence of which would render the tumor incompletely resectable. The second step is to incise peritoneum with a sufficiently deep margin of normal body wall to provide a plane of dissection posteriorly to the spinous processes (Fig. 7). If at this point the surgeon can touch his fingers together bimanually *via* the two dissection planes and find an absence of interviewing tumor, the sarcoma is usually resectable.

A solid or hollow organ attached to the neoplasm should be considered potentially invaded and that normal structure, or portion thereof, should be resected *en bloc* with the specimen, which may include kidney, spleen, gallbladder, and portions of the diaphragm, liver, stomach, pancreas, gut, and so on. In general sarcomas do not directly invade major vessels, nerves, or bone. However su-

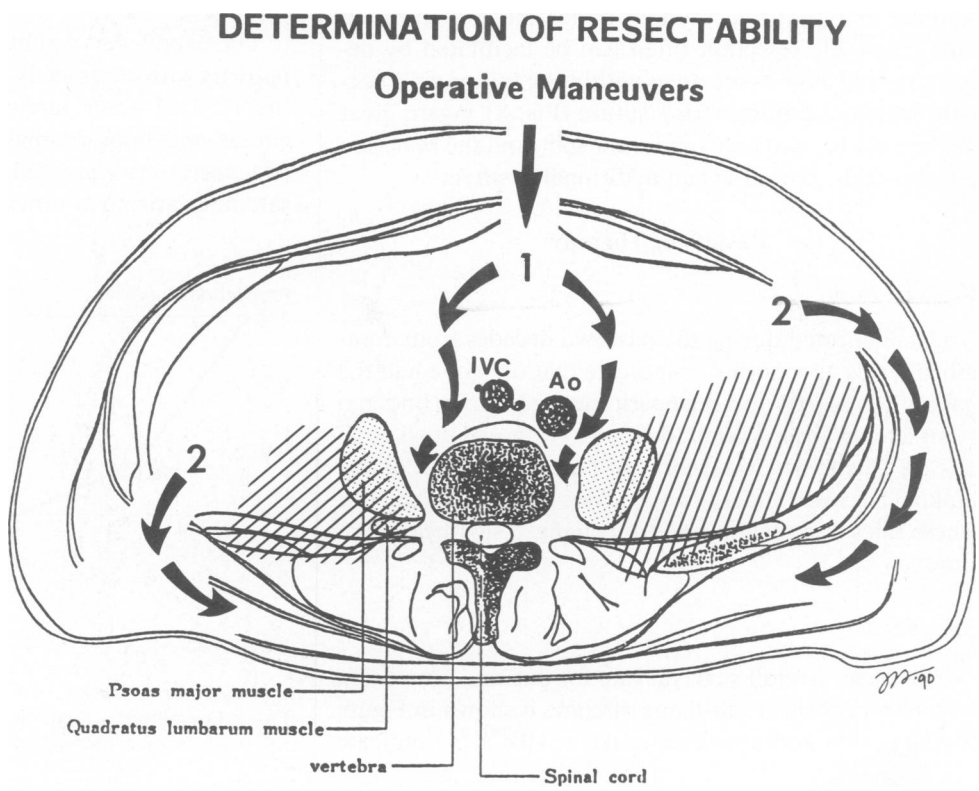

FIG. 7. Initial intraoperative maneuvers to assess resectability, particularly regarding evaluation of areas adjacent to spinal foramena.

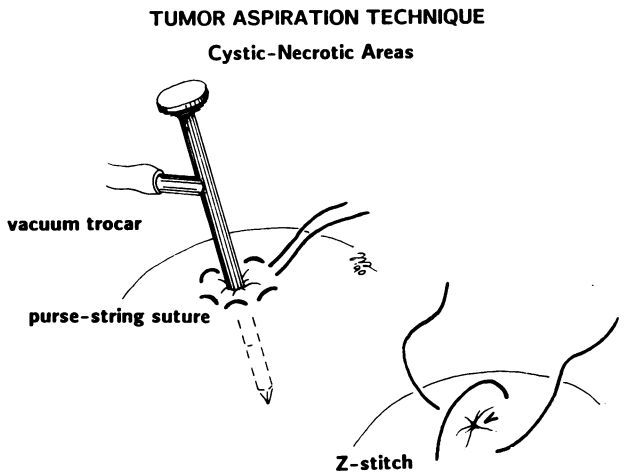

FIG. 8. Decompression of cystic tumor area using aspirating trocar and purse-string suture; an additional Z stitch is used to bury the puncture site.

badventitial, subperineural, and subperiosteal dissections may provide the only margins. Because of the development of extensive venous collaterals from vena caval compression, the vena cava can be resected safely without reconstruction in most cases. Aortic resection and replacement may be required in selected patients with very rare sarcomas arising from or encasing this structure.

Retroperitoneal sarcomas are frequently under extreme pressure and can be quite tense. This fact, when associated with large areas of liquefactive necrosis, makes tumor dehiscence likely during even minimal manipulation. In such cases safe resection often can be facilitated by decompressing large cystic areas within the tumor *via* a vacuum trocar and purse-string suture (Fig. 8). Again great care should be used to avoid tumor spill, and the puncture site should be buried *via* an additional Z stitch.

Results of Therapy

Resectability

Data collected during the past two decades from combined series (n = 560)[2,5–11] indicate that only one half the patients explored for retroperitoneal sarcoma undergo complete tumor resection, defined as removal of all gross disease (Table 3). Some form of partial resection or debulking has been undertaken in about one fifth of patients. These rates of resection have not changed significantly in time.

Survival

The mean overall survival rate for patients presenting with retroperitoneal soft-tissue sarcoma is shown in Figure 9. Data from combined series (n = 410)[4,6–9,11] indicate 2-, 5-, and 10-year survival rates of 56%, 34%, and 18%, respectively.

TABLE 3. *Resectability Rates*

Author (reference)	Study Dates	No. Pts.	Resection		Biopsy Only
			Complete	Partial	
Braasch and Mon[5]	1937–1967	37	15	7	15
Cody et al.[6]	1961–1971	34	13	21*	
	1971–1977	68	45	23*	
Storm et al.[2]	1964–1979	54	33	5	16
Karakousis et al.[7]	1957–1980	68	27	7	34
Dalton et al.[8]	1963–1982	116	63	25	28
McGrath et al.[9]	1964–1982	47	18	18	11
Glenn et al.[10]	1975–1983	50	37	8	5
Jaques et al.[11]	1977–1987	86	43	34	9
Total		560	294 (53%)	104 (19%)	118 (21%)

* Includes both partially and nonresected tumors.

The mean overall survival rate of patients undergoing complete (n = 240) *versus* incomplete (n = 228) resection is shown in Figure 10.[6–9,11,12] Even with complete resection, only slightly more than one half the patients survive 5 years. At each point in time, patients who have had resection of all gross disease have fared significantly better than those not completely resected.

Further analysis of patients who underwent incomplete resections appears to indicate some advantage to partial resection over biopsy alone at 2 years (52% *versus* 25% overall survival), but any benefit seems to be lost by 5 years (Fig. 11).[7,9,11]

The overall survival by histopathologic tumor grade of patients with completely resected disease is shown in Figure 12. Low-grade sarcomas, which tend to be fibrosarcomas and liposarcomas, appear to have an improved prognosis over high-grade (G2, 3) lesions,[2,6,8] as is true of sarcomas arising at other sites.

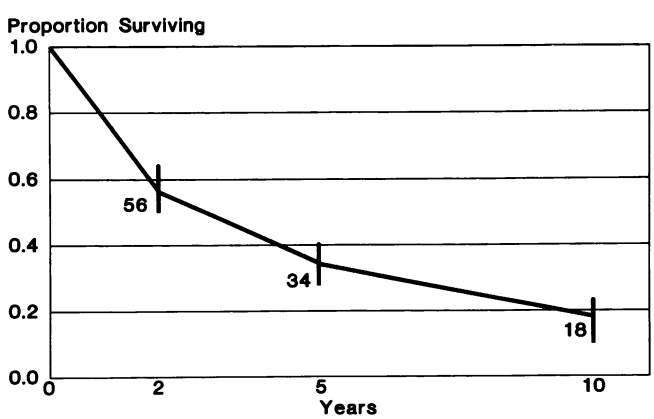

FIG. 9. Overall survival rates in patients presenting with retroperitoneal soft-tissue sarcoma (averages and ranges from cumulative series, n = 410).

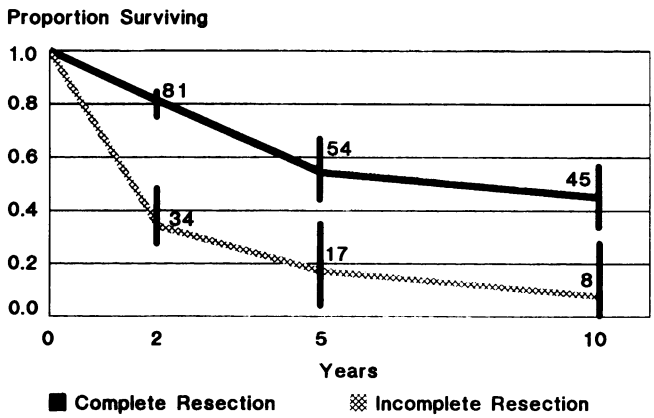

FIG. 10. Overall survival rates by extent of resection. (Averages and ranges from cumulative series. Complete resection, n = 240; incomplete resection, n = 228.)

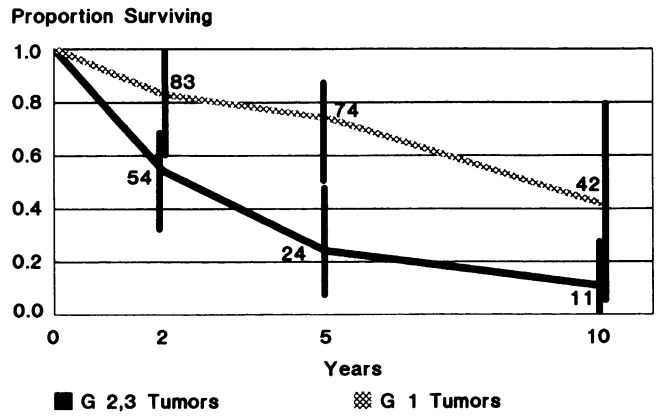

FIG. 12. Overall survival rates by histopathologic tumor grade in completely resected tumors. (Averages and ranges from cumulative series. G1 tumors, n = 49; G2, 3 tumors, n = 80.)

Recurrence After Complete Resection

Unfortunately more than 90% of patients undergoing successful removal of all gross tumor develop locally recurrent disease by 10 years (Fig. 13).[2,6–9,11] Because on the average only one third of patients ever manifest distant disease (the vast majority in liver or lung), local recurrence is the usual cause of death.[2,8,9,11]

Results of Adjuvant Radiation Therapy

Adjuvant radiation therapy has been used by several centers after complete resection (Table 4). External beam radiation appears to have had no impact on local control or survival,[6,7,9,10] which has been thought to be due to dose-limiting toxicity of the bowel. Unfortunately intraoperative radiotherapy (IORT) combined with external beam therapy to an accumulative dose of 60 Gy has also resulted in a similar pattern of local failure and no improvement in survival to date.[13]

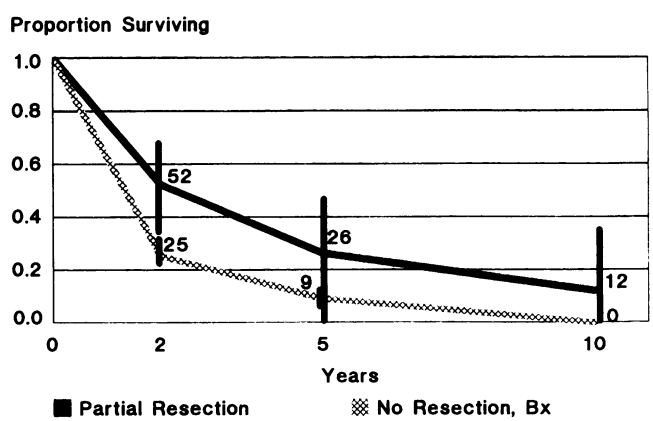

FIG. 11. Overall survival rates by extent of incomplete resection. (Averages and ranges from cumulative series. Partial resection, n = 59; biopsy only, n = 54.)

Results of Adjuvant Chemotherapy

Few trials exist using adjuvant chemotherapy combined with complete resection. Doxorubicin-based regimens, historically shown to have significant activity in metastatic sarcoma,[14] have had no impact on survival in the adjuvant[10] or neoadjuvant setting[2] on primary sarcomas arising in the retroperitoneum (Table 5).

Future Priorities

More than 90% of patients with completely resected retroperitoneal sarcomas fail locally. Unfortunately it is unclear from published series whether tumors recur after total resection with negative microscopic margins. It is also unknown what margin is necessary to achieve tumor clearance. The role of partial resection in these highly vascular and frequently necrotic tumors has also yet to be defined. For these as well as a number of other obvious reasons, a national retroperitoneal sarcoma registry needs

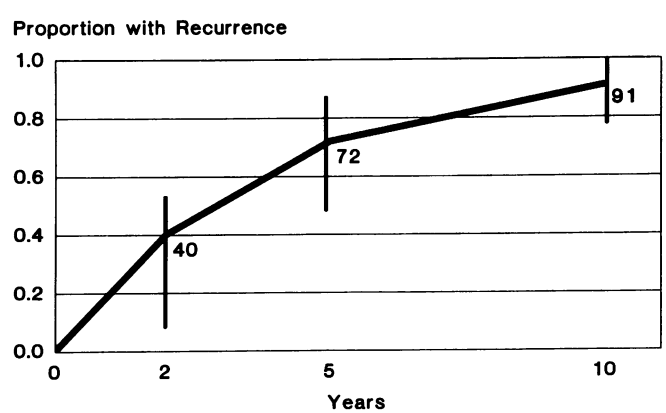

FIG. 13. Incidence of local recurrence after complete resection (averages and ranges from cumulative series, n = 204).

TABLE 4. *Postoperative Adjuvant Radiotherapy After Complete Surgical Resection*

Author (reference)	Study Dates	No. Pts.	Overall Survival: Surgery Alone (%)	Overall Survival: RT ± Chemo (%)	Overall Survival: Intraop RT (%)	p Value
Cody et al.[6]	1951–1974	38	30	53	—	NS @ 5 yrs.
Karakousis et al.[7]	1957–1980	27	75	75	—	NS @ 5 yrs.
McGrath et al.[9]	1964–1982	18	75	50	—	NS @ 5 yrs.
Glenn et al.[10]	1975–1980	37	43*	43	—	NS @ 3 yrs.
Kinsella et al.[13]	1980–1985	35	43*	48	48	NS @ 3 yrs.

* Survival at 3 years from cumulative surgical series, n = 80, high-grade tumors.[2,6,8]

NS, not significant; RT, radiation therapy; Chemo, chemotherapy.

TABLE 5. *Adjuvant Chemotherapy with Complete Surgical Resection*

Author (reference)	Study Dates	No. Pts.	Overall Survival: Surgery Alone (%)	Overall Survival: RT Alone (%)	Overall Survival: Chemo (± RT) (%)	p Value
Glenn et al.[10]	1975–1980	37	54*	60	60	NS @ 2 yrs.
Storm et al.[2]	1976–1981	10	54*	—	60	NS @ 2 yrs.

* Survival at 2 years from cumulative surgical series, n = 80, high-grade tumors.[2,6,8]

NS, not significant; RT, radiation therapy; chemo, chemotherapy.

to be established to evaluate and track these unusual neoplasms.

A better understanding of appropriate biopsy techniques and intraoperative approaches on the part of the surgeon will clearly enhance resectability and therefore prolong survival; however the few recorded attempts to improve local disease control using adjuvant radiation therapy or chemotherapy have largely failed. It is certain that the bowel will not tolerate high-dose external beam radiation therapy and that IORT may obviate this toxicity. Regrettably no pilot studies or prospective randomized trials have existed to explore adjuvant or neoadjuvant combined radiotherapy plus chemotherapy, which has been found to be so useful in achieving local control (88 of 96 patients, 92%) and limb salvage (95 of 96 patients, 99%) in intermediate and high-grade extremity soft-tissue sarcomas.[15] Despite continuing advances in radiation delivery and the development of new chemotherapeutic agents that require testing, these rare tumors do not lend themselves well to individual institutional trials. It is apparent that collective efforts will be necessary to alter the course of this disease. Experts in the field need to establish a national intergroup study to develop strategies and innovative trials for effective treatment of these lethal tumors arising in the retroperitoneum.

References

1. Arlen M, Marcove RC. Retroperitoneal sarcomas. *In* Arlen M, Marcove RC, eds. Surgical Management of Soft Tissue Sarcomas. Philadelphia: WB Saunders, 1987, p 220.
2. Storm FK, Eilber FR, Mirra J, et al. Retroperitoneal sarcomas: A reappraisal of treatment. J Surg Oncol 1981; 17:1–7.
3. Neifeld JP, Walsh JW, Lawrence W Jr. Computerized tomography in the management of soft tissue tumors. Surg Gynecol Obstet 1982; 155:535–540.
4. Storm FK, Sondak VK, Economou JS. Sarcomas of the retroperitoneum. *In* Eilber F, Economou J, Sondak V, Morton D, eds. The Soft Tissue Sarcomas. Orlando: Grune and Stratton, 1987, pp 239–247.
5. Braasch JW, Mon AB. Primary retroperitoneal tumors. Surg Clin North Am 1967; 47:663–678.
6. Cody HS, Turnbull AD, Fortner JG, et al. The continuing challenge of retroperitoneal sarcomas. Cancer 1981; 47:2147–2152.
7. Karakousis CP, Velez AF, Emrich LJ. Management of retroperitoneal sarcomas and patient survival. Am J Surg 1985; 150:376–380.
8. Dalton RR, Donohue JH, Mucha P Jr, et al. Management of retroperitoneal sarcomas. Surgery 1989; 106:725–733.
9. McGrath PC, Neifeld JP, Lawrence W Jr, et al. Improved survival following complete excision of retroperitoneal sarcomas. Ann Surg 1984; 200:200–204.
10. Glenn J, Sindelar WF, Kinsella T, et al. Results of multimodality therapy of resectable soft-tissue sarcomas of the retroperitoneum. Surgery 1985; 97:316–325.
11. Jaques DP, Coit DG, Brennan MF. Soft tissue sarcoma of the retroperitoneum. *In* Shiu MH, Brennan MF, eds. Surgical Management of Soft Tissue Sarcoma. Philadelphia: Lea & Febiger, 1989, pp 157–169.
12. Laurence W Jr, Donegan WL, Natarajan N, et al. Adult soft tissue sarcomas: a pattern of care survey of the American College of Surgeons. Ann Surg 1987; 205:349–359.
13. Kinsella TJ, Sindelar WF, Lack E, et al. Preliminary results of a randomized study of adjuvant radiation therapy in resectable adult retroperitoneal soft tissue sarcomas. J Clin Oncol 88; 6:18–25.
14. Antman KH, Elias AD. Chemotherapy of advanced soft-tissue sarcomas. Semin Surg Oncol 1988; 4:53–58.
15. Eilber FR, Giuliano AE, Huth JF, et al. Intravenous versus intraarterial adriamycin, 2800r radiation and surgical excision for extremity soft tissue sarcomas: a randomized prospective trial. Proc Amer Soc Clin Oncol 1990; 26:309(Abst 1194).